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E D I T O R I A L

ANTIBIOTICS AND STAPHYLOCOCCI

THE medical profession, at the moment, is faced once again with a decision which becomes more critical each time it arises. This decision involves the proper use of certain new antibiotics presently effective against many pathogenic organisms including the perennial trouble-maker, *Micrococcus pyogenes,* better known as the staphylococcus.

One by one, we have seen new antibiotics come, conquer for a time, and ultimately fail in the eradication of this hardy and highly adaptable organism, and there is little reason to believe that some of the current, new antibiotics will not suffer the same fate in time. The extent to which they are used by the medical profession will determine largely just when we may expect them to lose their effect against this organism for the more frequently they are used, the sooner this day will come.

This whole matter is not simply one of academic interest and it is particularly serious in the hospital environment. Recently, studies have shown that hospital personnel, including physicians and nurses, are common carriers of staphylococci in their nasopharyngeal secretions and that these contaminate such items as their clothing. Many patients become infected in the hospital with these same staphylococci which, in many cases, are resistant to all the common antibiotics.

There was a time when most strains of staphylococci were highly susceptible to penicillin. This drug finally lost its effectiveness as resistant strains emerged which were totally unaffected even by massive blood levels. The broad spectrum antibiotics followed the same pattern, and all of us well remember how erythromycin—when it was first released—was remarkably effective against resistant staphylococcic infections. Evidence is accumulating today that erythromycin is becoming less and less useful for this purpose, particularly in those infections seen in the hospital where the incidence of resistant strains is much higher than in general practice.

We are fortunate in having at least two new antibiotics with great effectiveness against staphylococci and herein lies the difficult decision of which we speak. The busy physician, not wishing to take the time to determine the susceptibility of the causative organism in a given infection, is inclined to use the most recent and, therefore, most likely the best antibiotic available. At the beginning of such practice, he is rewarded by dramatic results and this still further adds to his inclination to follow this procedure. What he may or may not realize is that he is throwing in, at the outset, his last line of defense and that there will come a day when patients will die while he stands hopelessly and helplessly without an effective drug to use. This is true since the use itself of these new antibiotics is the thing which sets in motion the chain of events leading to the development of resistant strains.

So far, we have been fortunate since the tremendous research activity in our pharmaceutical laboratories has provided us with a new antibiotic at regular intervals. There is serious doubt whether we can expect a continuation of this parade of new agents at regular intervals. In some countries, this problem has been met by government regulations restricting the use of certain antibiotics to those cases caused by resistant strains. Such regulations undoubtedly greatly prolong the utility of the antibiotic so restricted.

The pharmaceutical industry cannot be criticized for commercially exploiting each new development as it comes from their research activity. This, indeed, is standard practice. It is expected, however, that the medical profession would exercise a conservative approach rather than follow blindly a pathway which may not be in the long-range interests of their patients and the public at large.

L. F. Tice

THE CASE FOR PHARMACY LAW ENFORCEMENT *

By Robert L. Swain

THE assertion that our state pharmacy laws were enacted for the protection of the public is not likely to provoke controversy or incite criticism or denial. These laws are appropriately classed with public health legislation, a fact which in itself carries with it the express or implied meaning that they are necessary to safeguarding the health of our people in all matters involved within the term "professional pharmaceutical service".

These laws are regulatory of the practice of pharmacy. They set forth the character qualifications of persons seeking to enter the profession. They detail the educational and experience standards which prospective pharmacists must meet.

They limit the compounding and dispensing of prescriptions to persons who have satisfied the legislative requirements for membership in the profession. They demand evidence of competency and skill and the state itself issues a certificate testifying to such achievements. And, by way of positive assurance that the pharmacy is in the charge and under the direction of a professionally qualified pharmacist, the law commands that the State Board of Pharmacy certificate be prominently displayed in every pharmacy or drug store.

While there are many other provisions in our pharmacy laws bearing upon serving the public interest, those referred to here are amply sufficient for centering attention upon the great public purposes which these laws were conceived and ordained to serve.

At this point, some very significant questions press for consideration. If the pharmacy laws are intended to protect the public in matters pharmaceutical, should they not be actively enforced so as to accomplish this purpose?

If these laws restrict the compounding and dispensing of prescriptions to professionally qualified pharmacists, should not they be enforced so as to keep the unqualified from dabbling in prescription work?

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* Presented at the Conference of Boards and Colleges of Pharmacy of District No. 2, Atlantic City, N. J., October 25, 1956.

If these laws demand that a pharmacy must at all times be in charge of a registered pharmacist, should they not be enforced so as to assure the public that every pharmacy is conducted in compliance with this legislative demand?

Should not our pharmacy laws be administered and enforced fully to meet the legislative intent and purpose that the public must be protected against the dangers which go hand in hand with the untrained, uneducated, and incompetent meddlers in pharmaceutical practice?

The mere raising of these questions gives rise to the logical and reasonable answers. Of course, the pharmacy laws should be actively, practically, and properly enforced!

Of course, the public welfare demands that only the professionally qualified be allowed to practice pharmacy!

Of course, the public safety demands that prescription work be restricted to those who have satisfied the state that they are professionally competent to engage in this specialized professional practice.

Of course, the protection of the public demands that a pharmacy be in the personal charge of a registered pharmacist at all times!

Of course, the public interest demands that pharmacies be conducted in compliance with the requirements of the law so that the public may be shielded against the dangers inherent in the unqualified handling of drugs and medicines and the incompetent meddlers in pharmaceutical work.

But as we face up to the meaning, significance, indeed, the urgency of these questions, we are forced to admit that, by and large, the enforcement demanded simply does not exist.

In some states a reasonably efficient law enforcement program is in effect while in most of the others it is sketchy and nebulous, to say the least. Indeed, it can be said that in far too many states, nothing approaching adequate enforcement of our pharmacy laws exists or is even claimed to exist.

It would be well for us to come to grips with the inevitable consequences of our failure to enforce and administer our pharmacy laws in the interest of the public. Indeed, we should also see this failure in terms of its adverse effect upon pharmacy and as detrimental to our own personal and professional welfare.

When we permit the unregistered Toms, Dicks and Harrys to meddle with our professional pharmaceutical duties, do we not show

in the most positive manner, that it makes little difference who performs them?

When we allow the unqualified, the untrained, and unregistered store personnel to dabble in prescription work, do we not proclaim far and wide that such work does not require high professional qualifications, and hence is not of any special importance either to ourselves or the public? When we leave our pharmacies in charge of untrained and unqualified employees do we not put ourselves on record to the effect that conducting a pharmacy is a commonplace undertaking and that it matters little to the public anyway?

If we conduct our pharmacy merely as a run-of-the-mine store, do we not shear it of any promise of being seen by the public in any other light?

It has long been my fixed conviction that the public will accept pharmacy at the face value we ourselves give it. If we deal with it on a high professional plane, the public will accept it in like manner. If we show by our daily work and in all the details of our operations that we do not regard it highly, that we frequently play fast and loose with it, that we condone violations of the law as of little public signficance, there is complete certainty that the public will agree with our points of view.

The time has come for us to recognize that our standing with the public is tied in, to some degree at least, with our compliance with the requirements of the pharmacy law and with our manifesting that kind and degree of professional responsibility inherent in the aims and purposes of the act.

Stated in a different manner, we serve our basic public relations interest by open and full compliance with the public protection purposes of the pharmacy act. And, conversely, we injure our standing with the public when we manifest a callous attitude to the fundamental aims, purposes, and objectives for which the pharmacy act was enacted.

It has long been my conviction that we have been negligent in our obligations both to pharmacy and the public by not regarding our pharmacy laws as a great professional, indeed, competitive asset.

If the state itself has found it imperative to enact legislation for the protection of the public in matters pharmaceutical, common sense would seem to demand that we conduct our pharmacies and ourselves in such a manner as to show the public that we do afford the protection for which the law stands.

Indeed, it might be well for us to predicate our public relations efforts, in part, upon the broad public purposes of the pharmacy laws, their significance to us, our significance to them, and our determination to have them reflected in our day to day professional conduct.

As a practical matter, what are the essentials of an adequate pharmacy law enforcement program? What are its indispensable needs?

First of all, our state boards should be financed so that they can inaugurate and maintain an adequate enforcement program. It seems both illogical and unfair to vest the boards with the affirmative duty to regulate the practice of pharmacy and to enforce the pharmacy law in the public interest without providing them with funds necessary to the performance of this duty!

It is highly desirable that steps be taken to provide the board with a full-time secretary or executive official. There are, admittedly, many high principled pharmacists serving as board secretary and at the same time trying to conduct a retail drug store.

Obviously, one or the other must suffer. Meeting the legislative obligations inherent in directing a state agency such as a board of pharmacy is a full-time job in the most accurate use of the term. Conducting a retail drug store in these times when the overall pattern of retail distribution is undergoing revolutionary changes and when the drug store is beset and belabored with intense competition from all sides demands one's full and complete resources.

The board should also have a sufficient number of inspectors essential to doing a reasonably effective field job. It can be shown affirmatively that in those states where the board is adequately financed, where the executive officer is on a full time basis, and where inspection is carried on as a definite part of the board's activities, the basic purposes of the law are achieved.

A short time ago, a board of pharmacy secretary discussed with me the enforcement situation in his state with the statement that the board, as now functioning, was not able to do any enforcement worthy of the name. He himself conducts a successful retail pharmacy. The board's income is so low that it is hopelessly unable to meet the enforcement needs in the state. No inspectors are employed. The few inspections which are made are done by the individual board members when they can steal enough time from their stores in order to spend a few hours on the road.

To state that this secretary is frustrated, concerned, and about ready to resign his commission is merely to state what he himself

admitted to me. That situations like this, or closely similar, exist in many states is well known to us, if not to the public. That such situations, wherever they do exist, are fraught with highly dangerous potentialities, is a matter which should give us real concern.

Indeed, we might well face up to the question as to how long can pharmacy assume the risks inherent in such situations? How long can a board of pharmacy safely accept responsibilities which it is in no position to meet?

How long can we defer positive steps to acquaint the public, the legislature, and the administration in each state of the need to put the board in position to discharge the obligations which the public welfare has imposed upon it?

Now, in this discussion, my purpose has been to focus attention upon the fundamental character of law enforcement and to make us critically aware that no adequate enforcement programs are now in effect in many states. My purpose has also been to emphasize that boards of pharmacy are burdened with positive and affirmative duties which they are in no position to perform, and that steps should be considered for meeting these most glaring defects in our whole board of pharmacy operation.

In connection with this over-all subject some thought should be given to what is the best enforcement agency and to a comparative analysis of the enforcement methods and procedures now in use.

This would call for a discussion of the public health aspect of law enforcement, the competitive status of board of pharmacy members, the need to have enforcement work totally devoid of the competitive tint, and undertaken as a matter having a vital relation to public health and public safety, and other factors inherent in a well conceived, well balanced law enforcement activity.

But, covering this phase of our subject calls for considerations and evaluations not possible in this address. It is, however, one to which I intend to give thoughtful attention and hope to present my views on some subsequent occasion.

By way of preview of this later paper, however, it might be well to stress that board of pharmacy members are required by law to be actively engaged in retail pharmacy. Virtually all of them own and operate their own retail pharmacies.

This means, of course, that they are in competition with other retail pharmacists, particularly when they are located in the same town or neighborhood.

It means, too, that they are in competition with supermarkets and other large mass outlets which are now engaged in a relentless competitive battle aimed at building more and more volume in basic drug store merchandising products and lines.

This competitive status has, in some instances, had its impact upon pharmacy law enforcement. I have heard board of pharmacy members call for overlooking violations in their own town or neighborhood because any unpleasant outcome would react against them.

True, the pharmacy act was not being observed, prescriptions were being filled by non-registered personnel, the store was frequently without a registered pharmacist, but even so, the board member did not want to be tagged with having the offenders prosecuted, simply because he and the violating pharmacist were friendly competitors, living in the same town, and had known each other for a long time.

The competition factor needs to be considered when a board, made up of retail pharmacists, seeks to curb a supermarket or some similar outlet from selling products which, in the opinion of the board, should be sold only in retail drug stores.

The attorney for the defense stands a good chance of putting the board in an adverse light when he brings out that the non-pharmacy dealer is in competition with retail pharmacists and that the board itself is made up of retail pharmacists.

The attorney for the defense might attempt to show that the alleged prosecution is little more than a competitive matter, and that the board is more concerned with keeping the business for pharmacists rather than with any real concern over the public health nature of the violation.

Indeed, I have sat through court hearings in which this precise practice was indulged in by the defense. Now, of course, courts can be counted upon to get at the bottom of all prosecution cases, but even so, the mere fact that sometimes the board members can be cited as parties in interest to the issues involved has had an unfortunate impact upon the outcome of board of pharmacy cases.

The whole pharmacy law enforcement program would seem open for reappraisal and readjustment in the light of the wide-spread handling of drugs and medicines by highly aggressive non-drug outlets whose sole purpose is to build more and more volume.

As these outlets broaden their drug store sections, as they seek to make them more inclusive, more representative, it seems likely that they will tend more and more to encroach upon these drug and

medicinal product categories which boards of pharmacy have every reason to believe should be limited to professional hands in the interest of the public health and safety. This fact, and the potentials inherent in it, need to receive the closest study in its relation to any well conceived pharmacy law enforcement program.

All of which would seem to suggest the wisdom of seeking some means of having violations of the pharmacy laws prosecuted as to bring out in bold relief the public health hazards inherent in the violation. If such violations could be considered in the light of public health or as highly detrimental to the public health and safety, with the competition phase completely eliminated, pharmacy might gain in some highly significant respects.

But, as I remarked above, a full analytical discussion of this matter must be deferred to a later date and to some future occasion.

In conclusion, let me emphasize that nothing that I have stated in this paper is intended to give the slightest approval to consolidated boards such as we now have in effect in some states. These bodies have proved themselves aloof to and disinterested in effective enforcement and virtually none worthy of the name is being done in those states in which the examining and enforcing agencies have been scrambled into one overgrown agency.

The enforcement job I have in mind is one for us as alert members of our profession, and as fully alive to the need to afford the public the protection which forms the woof and fabric of our pharmacy laws.

The job is ours. The responsibility is ours. The obligation is ours.

It is my devout hope that we may see this over-all subject in the proper light and in the truest perspective. We can serve our profession and the public interest in no more compensating way.

A NEW IODINE DAIRY SANITIZER

By Louis Gershenfeld *

THE problems in milk sanitation, from farm to consumer, are of considerable magnitude. In fact, in many areas throughout our country, they are comparatively new and in others have not even been presented. Space does not permit to point out even the highlights or to indicate the numerous reasonable sanitary regulations promulgated today for the guidance of all concerned.

Sanitary Control

There always is a need for sensible and up-to-date regulations for proper control relating to sanitation and especially as it concerns dairy sanitation and food service. Everyone shares in the benefits of proper sanitary procedures. Until better methods of sanitary control for better evaluating the whole structure of sanitation are introduced, we cannot relax our guard against current accepted methods nor lessen our campaign against indifference nor slacken our crusade against laxity. It is not sufficient to merely have the necessary sanitary facilities. They must be maintained at all times in a sanitary condition.

Sanitary Inspections

Modern methods have proven that many and varied operations are necessary if it is desired that a wholesome and safe fluid milk is to be marketed. It cannot be emphasized too strongly that sanitary inspections all along the line from the producer on the dairy farm to the consumer as well as constant laboratory control are absolutely essential. Pasteurization is an important additional safeguard. With these, there also is needed an effective program of education (or supplying information) to be assured that high standards of sanitation and

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the best of housekeeping cleanliness are being practiced. The end-result is an effective display of positive sanitary attitudes in action.

Inspections versus Sanitization

It must be recognized that often even a careful sanitary inspection will not always disclose exact operating conditions and especially a complete knowledge of day-to-day performance. Even if the findings of a sanitary inspection appear highly satisfactory, there is no assurance that they will continue so. We also must recognize that the sanitary inspection staff has not increased in proportion to the increase in the volume output of fluid milk and dairy products or in the number of places to be inspected. After all, the real hazard in this over-all picture is human frailty, something frequently difficult to detect even with most careful inspections. It is believed, however, that in the use of an effective sanitizer for equipment, utensils, etc., as the final step even though they have been properly cleansed, there is an additional aid and safeguard possessing noteworthy possibilities for assuring a better sanitary quality of fluid milk. We must never overlook the fact there may be new and even better methods of handling old problems, especially as it concerns the elimination of danger potentials. Employing an effective sanitizer must never be used as an excuse for careless, indifferent and insanitary methods for the production of market milk. Sanitization procedures where possible, as in the case of pasteurization, are additional safeguards.

Sanitizers

In the author's laboratory interest concerning preparations of iodine as antiseptics, bactericides and sanitizers, has extended over several decades (1). Recently attention was directed to a clinical investigation of a new iodine preparation by Ryan et al. (2), who suggested that this product "Heliogen may prove to be a valuable addition to the chemotherapeutic agents used in the treatment of wounds". In our laboratory we conducted *in vitro* studies and reported that solutions of this iodine product "are bactericidal against the commonly found vegetative forms of bacteria apt to be encountered in body tissues, the oral cavity, vaginal tract, etc. and at varying pH ranges and temperatures either in the presence or absence of blood serum" (3, 4). A later *in vitro* study indicated that Poliomyelitis Virus (all

three types) was inactivated by freshly prepared Heliogen Solutions (5). Clinical evaluations revealed the efficiency of the latter containing diatomic iodine as a mouth rinse (6), as a gargle for acute and chronic infections of the throat (7) and as an oral lavage (8).

Heliogen Dairy Sanitizer

More recently, the author's laboratory has been interested in iodine as a sanitizing agent and several articles have appeared (9, 10, 11, 12, 13, 14). Public Health authorities all over the country have approved the use of iodine in sanitization procedures. Extensive studies have been and are being conducted on all available iodine sanitizers on the market. To this list, Heliogen Dairy Sanitizer now available, has been added, having reported above the usefulness of the same active ingredient, diatomic iodine, as an antibacterial agent. This diatomic iodine dairy sanitizer is marketed in individual sealed, metal foil envelopes each containing one-half ounce of the product, the active ingredients (44%) being Potassium Iodide and Chloramine-T. When the contents are dissolved in 10 gallons of water, 65 p.p.m. of active diatomic iodine are released. It is of interest to note that as a solid and in individual sealed packages, there is ease in storage and manipulation. The powder is white, odorless and stable and all packages can be stock-piled. The contents do not stain directly and being a solid, there are no problems as to freezing. It, of course, is possible to package smaller or larger quantities to make available any desired dilution when added to water.

Numerous toxicity studies have revealed that Heliogen Dairy Sanitizer possesses a comparatively low toxicity. Repeated Insult Patch Testing resulted in conclusions that solutions of this diatomic iodine sanitizer are not apt to cause dermatitis. Using the "Available Chlorine Germicidal Concentration" procedure (17), a capacity technique, details of which will be published later, the use-dilution of 65 p.p.m. of diatomic iodine derived from Heliogen Dairy Sanitizer was effective against at least six increments of cultures of the test bacteria (*Micrococcus pyogenes* var. *aureus* and *Salmonella typhosa*) both at 20° C. and 5° C. This was more effective as compared with chlorine (200 p.p.m.) under identical conditions of testing. Using the Weber-Black technique (18), the same use dilution displayed a 100 per cent kill within 15 seconds (*E. coli* as the test bacterium), both at 20° C. and 5° C. This was more effective as compared with chlorine under identical conditions of testing.

Field Tests

It is common knowledge today in the medical sciences that a drug can only be regarded as suitable for the purposes recommended, providing in the final analysis clinical investigation proved its efficacy. This is required regardless of the most favorable findings obtained in laboratory studies (both *in vitro* and *in vivo* investigations). In like manner properly supervised field studies under practical use conditions must be made so as to evaluate and to enable one to make qualitative and quantitative judgments and appraisals concerning disinfectants, sanitizers and similar agents, even though laboratory tests of all kind reveal most satisfactory findings. These as practical tools of measurement for adequate sanitation can contribute significantly and serve as a satisfactory means of evaluation of the methods used in practice.

In a detailed report which will be published later, extensive field tests have been and are being conducted by the Philadelphia Dairy Products Company, Inc. under the supervision of Richard S. Doughty, Director of Products Control. These studies were to determine the effect of a solution of diatomic iodine (65 p.p.m.), as made available by Heliogen Dairy Sanitizer, upon the bacterial population of raw milk produced on farms, after employing this diatomic iodine sanitizing solution on strainers, pails, air hoses and all other equipment used directly or indirectly for milk production. As a safety factor, the high concentration of 65 p.p.m. of diatomic iodine was used. In the selection of producers, all kinds were encountered. Farms giving bad, good and variable findings in the past by the conventional chlorine sanitizers were chosen. Approximately 25 different patrons were involved and approximately 600 different tests were made. Complete details will be presented later, but in a preliminary report the Philadelphia Dairy Products investigators indicate that with Heliogen Dairy Sanitizer used on the farm as a sanitizing agent, the bacterial content of the raw milk is markedly reduced as compared with conventional methods in use. It is apparent from the results of this field study that the use of Heliogen Dairy Sanitizer makes available a milk for marketable purposes of exceptional quality.

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CLINICAL STUDIES ON ANTICANCER AGENTS. X.

By John R. Sampey *

THE increased interest in the management of cancer is reflected in the 1315 references reviewed in this paper and earlier studies (190). In this study investigations on the use of radiogold and radiophosphorus dominate the inorganic chemicals, while nitrogen mustards and TEM lead among the organic nitrogen compounds. Sex hormones and the adrenals continue to lead all fields in the search for anticancer agents. The employment of antibiotics and the psychological problems of the cancer patients are growing fields in the clinical control of neoplasms.

I. Inorganic Chemicals

Radiogold. Au_{198} has been used extensively in the management of neoplastic effusion (8, 10, 41, 45, 51, 117, 121, 152, 153, 197, 213, 214, 236). Brain tumors (154, 219), and cancer of the cervix (5), prostate (162, 163), bladder (68, 158), and skin have responded to radiogold therapy (167). Rominger (184) employed this isotope in cases of surgical complications, and Fellinger and Vetter (74) noted good remissions in chronic myeloid leukemia.

Radiophosphorus. P_{32} induced remissions in chronic leukemia (27, 33, 65, 142), polycythemia vera (1, 96, 99, 230, 237), prostatic carcinoma (187), mycosis fungoides (157), carcinoma of the tongue (16), epibulbar melanoma (124), and pleural effusions (109).

Radiocobalt. Bladder neoplasms responded to Co_{60} therapy (16, 111, 140, 231). This isotope also caused longer survival in patients with glioblastoma multiforme (120), and bronchial carcinoma (77).

Radioiodine. Several studies described the palliative results in the treatment of thyroid neoplasms with I_{131} (46, 52, 118, 185, 208, 225).

Radiostrontium. Sr_{89} increased the survival of patients with eye neoplasms (124).

* Furman University, Greenville, South Carolina.

Radiotantalum. Wallace, et al. (235), reported little response from Ta_{182} treatments for bladder carcinoma.

Radioyttrium. Effusions due to neoplasms responded to Y_{90} (207).

Radon Seeds. Radon seeds have been applied in the management of bladder tumors (71), and retinoblastoma (210).

Phospho-Acids. Phosphotungstic and phosphomolybdic acids induced necrosis of carcinoma in patients (150).

II. Organic Nitrogen Compounds

Nitrogen Mustards. Nitrogen mustard therapy has been successful in the management of Hodgkin's disease (50, 56, 75, 83, 130, 165, 176, 178), lymphosarcoma (21, 43, 165, 176), carcinoma of the liver (239), nasopharyngeal carcinoma (212), subacute erythemia myelosis (188), and lung neoplasms (32, 141). Combined with X-rays it induced remissions in lung cancer (17), and advanced neoplasms of the urinary tract (228). Nitramin caused remissions in malignant hemopathies (48).

TEM. Triethylene melamine therapy gave remissions in leukemia (55, 76, 99, 126, 136, 145, 155), Hodgkin's disease (76, 125, 136, 155, 226), and lung neoplasms (94, 128, 189), liver (239), and ovary (218). Lymphosarcoma (127), nasopharyngeal carcinoma (122), and polythemia vera (237) also responded to TEM therapy.

6-MP. 6-Mercaptopurine is finding increasing usefulness in the treatment of acute leukemia (64, 70, 114, 159, 192).

Amines. Naphthyl-dichloroethylamine was effective in Hodgkin's disease (232), and polycythemia vera (174). Chronic leukemia responded to beta-mercaptoethylamine (9).

Phosphoramide. TETPA induced objective remissions in a number of neoplasms (14, 15).

Sulfonamide. Sulfonamide combined with irradiation prolonged the lives of patients with metastatic seminoma (138).

Azaguanine. Guanazola inhibited acute leukemia (47).

Ethionine. This amino acid was without conclusive results in the treatment of cancer of the pancrease (97).

Urethan. Nasopharyngeal carcinoma responded to urethan (122, 212).

TMM. Trimethyl melamine gave good results with Hodgkin's disease, chronic lymphatic leukemia and breast carcinoma (199).

III. Folic Acid Antagonists

Aminopterin. This antagonist has proved effective in acute leukemia (98, 114, 116, 191, 192), Hendricks and Fowles (100) reported aminopterin most effective with subacute lymphocytic leukemia, but ineffective with acute fulminating type.

Amethopterin. This antagonist paralleled aminopterin in its action with leukemia (52, 70, 100, 114).

Daraprin. This antimalarial drug with antifolic properties lowered the red blood cell count in polycythemia vera (107).

IV. Hormones

Estrogens. Etrogens have been employed extensively in the management of prostatic cancer (13, 20, 29, 42, 52, 63, 81, 84, 95, 101, 110, 112, 134, 143, 146, 147, 151, 160, 168, 227), and breast cancer (79, 87, 115, 164, 195, 216, 240). Estrogens also gave palliative results in neoplasms of the cervix (85, 106, 148), lungs (131), and rectum (72). Gagliardi (82) advised against the use of stilbene in the treatment of the uterus.

Androgens. A number of clinical studies have been made on the control of breast neoplasms with androgens (18, 30, 79, 92, 115, 133, 164, 173, 179, 198, 216, 240). Testosterone therapy has also been used in hypophyseal adenoma (34), genetal cancer (229), corpus uteri carcinoma (106), lung metastases (131), and prostatic cancer (95). Jentzer (110) noted that autopsy findings show natural hormones are more effective in prostatic cancer than synthetic ones. Gibson (90) observed no decrease of prostatic cancer by circumcision.

Adrenalectomy. Carcinoma of the prostate (11, 24, 38, 57, 80, 149, 194), and breast cancer (31, 35, 38, 57, 66, 103, 104, 123, 177, 216) responded to adrenalectomy.

Cortisone. Cortisone therapy is finding increasing usefulness in acute leukemia (39, 70, 98, 114, 116, 135, 159, 191). This hormone

caused remissions in Hodgkin's disease (135, 193), and carcinoma of the prostate (134, 146). Kittredge (119) warned of potential hazards of cortisone therapy in prostatic cancer.

ACTH. Acute leukemia (39, 98, 116, 159, 191, 222), and Hodgkin's disease (135, 222) responded to ACTH treatments.

Hypophysectomy. Removal of the hypophysis gave promising results in breast cancer (62, 87, 132, 169, 170, 172), and prostatic cancer (132, 170), and testicular cancer (91). Archer (7) found no cases in medical literature of cancer of the breast or ovary in Simmonds' disease (hypopitiutarism).

Follicular Hormone. Breast carcinoma (61), and corpus uteri carcinoma (106) responded to this hormone.

V. Miscellaneous Agents

Antibiotics. Actinomycin and actinomycin C proved effective in the treatment of Hodgkin's disease (28, 53, 89, 105, 139, 161, 201, 202, 220), lymphosarcoma (53), lung metastases (200), and malignant reticulosis (53, 93, 161). Penicillin therapy has been used in acute leukemia (192), Hodgkin's disease (40), and skin cancers (40). Ruppert (186) treated granuloma with terramycin, and Mickhailoff (144) used antibiotics and percoten for chronic lymphoid leukemia.

Psychotherapy. The psychological and emotional problems of the cancer patient are receiving increased attention (2, 22, 23, 30, 37, 44, 54, 59, 67, 69, 78, 88, 108, 156, 180, 181, 204, 205, 211, 217, 221, 224, 233, 238).

Colchicines. Hodgkin's disease (49, 129, 166, 215, 241), myeloid leukemia (49, 129, 166, 241), lymphosarcoma (215), lymphatic leukemia (215), lung carcinoma (241), and cancer of the cervix (73) responded to colchicine.

Diet. Tosetti (223) employed high vitamin A therapy with mistletoe extract for genital carcinoma. Sansone, et al. (192), secured partial remission in acute leukemia with antibiotics and vitamins. B_{12} and nitrogen mustards induced clinical improvement in subacute erythremic myelosis (188). Ries and Blasiu (182, 183) used vitamins with AF2 factor in treating various neoplasms.

Myleran. Chronic myeloid leukemia responded to myleran (98, 136, 234).

Podophyllin and Podophyllintoxin. Breast carcinoma (203) and myeloid leukemia (171) were treated with podophyllintoxin. Podophyllin had no effect on human adenocarcinoma of the bladder (36).

CB1348. N,N-di(2-chloroethyl)-p-aminophenylbutyric acid, CB1348, induced remissions in chronic lymphatic leukemia (6), and Hodgkin's disease (4).

Viruses. R.I.67 virus failed to affect 14 patients with advanced neoplasms (209), and Virus A and WEE viruses did not influence carcinoma of the palate in one patient (175).

Nitromin. Subjective improvement of 16 patients with carcinomas of the lungs, breast, etc., were noted after nitromin therapy (19).

Mustard Gas. This agent destroyed skin cancers (3).

Indigo Carmine. This dye induced gross and microscopic changes in carcinoma of the rectum (26).

Trichloroethylene. This halide showed a palliative effect on multiple myeloma and breast cancer (58).

Enzymes. Proteolytic enzymes of the nature of trypsin gave promising results in leukemia (86).

Chloropromazine. This agent afforded relief from nausea and vomiting caused by advanced neoplastic diseases (102).

Butalidon. This drug gave palliation to leukemic patients (113).

Chlorophyll. A 5% solution of chlorophyll caused subjective improvement in patients with carcinomas (137).

Choline. Choline esters and salts with irradiation gave palliative results in patients with metastatic seminoma (138).

A-Blastomase. A-Blastomase, a mixture of p-oxyphenylamine, 1,2-ketocycloheptane and a gold sol. gave palliation to patients with inoperable neoplasms (196).

Morphene and DAPT. DAPT made large doses of morphene safe for patients with advanced cancer (206).

Urecholine. This agent relieved pain in 21 of 37 patients with rectal carcinoma (25).

APF. APF, anabolism promoting factors, in the form of vitamins, antibiotics, milk, etc., has been used on a variety of neoplasms (12).

Transfusions. Several types of leukemia were helped by transfusions (60).

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THE HEALTH NEWS INSTITUTE *

Its Aims and Objectives

By Chet Shaw **

I am grateful for this opportunity to tell you something about the activities of the Health News Institute, to explain our aims and objectives, and to invite you to share in the benefits for all members of the health team that are sure to result from our labors.

As most of you already know, the HNI was set up at the beginning of this year to meet a specific need. That need was for an alert, vigorous news agency to speak for the entire health field. The pharmaceutical industry can well be proud that it saw this need clearly, and took forceful action toward meeting it.

The one question that is probably uppermost in your minds is why did we need such an agency? To answer that question, I would like to refer to the penetrating analysis of the public relations situation confronting the industry, made by George F. Smith, president of Johnson & Johnson, at the Forty-fourth annual meeting of the American Drug Manufacturers' Association last April.

As you probably know, George is chairman of the ADMA Public Relations Committee, which spearheaded formation of the HNI, and as such is grandpappy of the organization.

Those of you who may have attended the meeting will recall George's warning that public misunderstanding of the health field as a whole—including doctors, retail druggists, wholesale druggists, hospitals, pharmaceutical manufacturers, and everyone else involved—was "growing relentlessly and seriously."

The lack of any single unified voice for the industry, he pointed out, was allowing the whole field of medical public relations to go by default to those "all too eager to fill the gap with slanted truths, half-truths and misconceptions." But, said Mr. Smith, the picture could be radically changed through a sound public relations program geared to the highest possible standards of business conduct and practices. As he told the ADMA meeting:

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* Presented at the meeting of the Federal Wholesale Druggists' Association, The Greenbrier, White Sulphur Springs, West Virginia, September 17, 1956.

** Executive Director, Health News Institute, 60 E. 42nd St., New York 17, N. Y.

"We are on the threshold of changing a dangerous and threatening situation to one that can raise the prestige of the entire health team in the all-important sphere of public opinion."

The ADMA delegates quickly ratified the decision of their Executive Committee to launch the HNI, along with the 50-50 cooperation of the American Pharmaceutical Manufacturers' Association. Since then, other prominent organizations in the field have joined in underwriting our program, such as the Proprietary Association, the American Pharmaceutical Association, and the National Association of Retail Druggists. Other associations will act as their conventions are held.

Now, you may well ask, what has the HNI accomplished so far?

After little more than six months of effort, the HNI can, I believe, take credit for a significant improvement in the highly complex field of health-team public relations. For one thing, recognition is growing daily among such opinion molders as newspaper and magazine editors, radio and television commentators, public officials and health industry leaders that HNI is THE agency to which to turn for the latest, most accurate information on health news. A steadily-increasing flow of inquiries and requests for information in recent months bears this out.

We also have initiated and released major stories on some of the most newsworthy developments in health to thousands of publicity outlets across the country. These include a thorough-going study of tranquilizer drugs: a report on the availability of Salk polio vaccine this summer, and detailed story on the success of isoniazid and other new drugs in treating tuberculosis. Others will follow from time to time.

In addition, we have supplied background material for speeches by many prominent persons in the health field; written articles at the special request of editors of almanacs and encyclopedias on various health-team matters, and supplied reprints of Mr. Smith's speech as well as other significant public addresses to editors and trade groups.

We have kept a watchful eye on the manner in which various forms of communications—newspapers, magazines, motion pictures, radio and television—deal with pharmaceutical and medical news, and have not hesitated to call the attention of those in authority to

what we feel are flippant or inaccurate statements about different members of the health team. In this regard, I refer specifically to our letter of protest to the producers of the movie "Bigger Than Life," which, we feel, unfairly portrayed the role of the doctor and pharmacist in the treatment of a patient. We hope in the future, as the HNI becomes even better known, to prevent such regrettable misconceptions to arise by heading them off at the source.

I am sure that all of you know Donald Cooley and his informative yet entertaining handling of pharmaceutical and medical news. At the kind invitation of the National Pharmaceutical Council, we have aided in distributing his newest booklet on prescription costs to the trade press, science writers, special editors and writers and trade associations.

We are cooperating with the Health Information Foundation on the preparation of a film showing the contributions to better health made by all members of the team. We also are preparing a fact book which will be an invaluable reference guide to health leaders in all sections of the country. Suggested editorials, drawing attention to the industry's contributions to better health, have been sent out to hundreds of newspapers, and more will follow.

One major project on which we are now working is to coordinate the releasing of health news during National Pharmacy Week, sponsored by the American Pharmaceutical Association, which will be observed this year from October 7th to 13th. We hope that all pharmaceutical companies will be able to release whatever current news stories they have during this period, to focus attention on the week and to increase public appreciation of pharmacists. With the cooperation of NBC, we are also producing a nation-wide radio show to dramatize the life of a typical pharmacist.

Now, if I may, I would like to tell you of a recent incident that seems to sum up exactly why the Health News Institute is needed.

Recently, we learned that the science editor of a large Eastern metropolitan daily newspaper was preparing an article on pharmaceuticals. We immediately contacted him and offered our assistance.

We quickly learned that the reason for this article was a recent visit that the writer's city editor had paid to his doctor. On receiving the doctor's prescription, the editor exploded in wrath. He denounced pharmacists and pharmaceutical manufacturers, who, he said were getting rich at the expense of the public, and said there was no

reason why he should have to take so many "pills." He then ordered his science editor to write an exposé of the situation.

Such a blow-off seemed to us to be exactly the sort of reaction a sound public relations program should seek to prevent. With proper information, we felt sure that the editor would be grateful that the vast research and dedicated effort of pharmaceutical science had produced the very drugs needed to help him.

In this we had a good break. The science editor so summarily ordered to "expose" druggists and the drug industry, was, we found, understanding of the industry's efforts and contributions, and sympathetic toward the pharmaceutical field. He assured us it was his intent to write a sober, accurate story, backed up by such facts as the great decline in prescription prices for most "wonder" drugs. What he needed was our help.

He got it. We supplied information. In return, we were repaid by the writer's grateful comment: "Thank God, there is finally a central source where factual and interesting information can be quickly obtained." Every science writer in the country, he said, would be delighted to avail himself of our services when the word got around.

We are seeing to it that the word does get around.

With the amount of support it now receives, the Health News Institute already speaks for a large segment of the health team. As more and more organizations join in its support, that voice will be strengthened. The day is not far off when it will be heard throughout the land, speaking for those thousands of dedicated men and women—doctors, nurses, pharmacists, hospital workers, pharmaceutical manufacturers, and dentists—who work untiringly to make better health for all a reality.

Where, you might ask, does the wholesaler fit in this picture. Obviously, as a key member of the health team, he has a keen interest in anything that helps the team as a whole. What benefits the industry is clearly advantageous to every segment of it.

But the wholesaler has a particularly large stake in this effort. *His customer, the retail druggist,* is perhaps the most misunderstood and the most underrated of all. An alarming proportion of the public does not appreciate the highly important role that the local pharmacist plays in the advances against disease—in the better health that Americans of today enjoy.

One of the key objectives of Health News Institute is to build for the retail druggist the public recognition and respect that he so

richly deserves. Thus, directly for your customers and indirectly for you, HNI expects to do a job that has been too long delayed.

One of the many definitions of the science of public relations is that it's 90 percent doing right and 10 percent getting credit for it. In this regard, let me again quote from George Smith's speech here last spring:

> "No amount of publicity"—he said—"no matter how good it is, will whitewash unfavorable conditions that may exist in any part of the industry. Good public relations begin at home."

Well, we're pretty much convinced that the industry is doing right, and by a lot wider margin than 90 percent. It's our job now to see that we get credit for it. With your help, there is no doubt whatever that we will succeed.

SELECTED ABSTRACTS

The Resistance of Crystalline Compounds to Sterilization by Gases. Abbott, C. F., Cockton, J., and Jones, W. *J. Pharm. Pharmacol. 8:709* (1956). A "cold" sterilizing process, employing formaldehyde and ethylene oxide gases, was investigated for its effectiveness in the sterilization of thermolabile crystalline substances. Crystals of Rochelle Salt were prepared and tested for sterility. Selected crystals were placed in a roller mill containing a standardized spore powder (10^6 *Bacillus subtilis* spores per Gm.) and milled for one hour. The crystals were then exposed to formaldehyde gas for 6 hours.

Other crystals were prepared by crystallization from a mother liquor containing 10^6 spores of *B. subtilis* per Gm. of suspension. These crystals were also exposed to formaldehyde gas for 6 hours. The authors found that only 1.8 per cent of the crystals contaminated externally with the spore powder remained contaminated after exposure to the gas. However, 90.2 per cent of the crystals prepared by crystallization from the contaminated mother liquor, and thus internally contaminated, remained contaminated after exposure to the gas. Evidence for the inclusion of spores within the crystals was given by electron micrographs which showed spore-like objects on the fractured surfaces of crystals prepared from contaminated liquors.

The authors also found that the more rapidly the crystals were prepared the more likely spores would be included within the crystals. Spores of *B. subtilis* were found to be able to survive within the crystals for at least five months. Several other crystalline substances were prepared. Internally contaminated crystals were obtained of hexamine, ethylene diamine tartrate, lactose, glycine, sodium biphosphate and hexamethonium bromide, but not of sucrose, chloral hydrate, and sodium chloride. Ethylene oxide gas was also used to attempt to sterilize the crystals, with results similar to those obtained with formaldehyde.

The authors pointed out that, although heavy contamination was employed in these studies, internally contaminated crystals may also be obtained from ordinary manufacturing procedures where the mother liquor is only lightly contaminated. Gas sterilization procedures could not be relied upon to render such crystals sterile.

Observations on Antibiotics in a Market Milk Supply. Shahani, K. M., Gould, I. A., Weiser, H. H., and Slatter, W. L. *Antibiot. & Chemother. 6:*544 (1956). A survey was conducted to determine the prevalence of antibiotics in market milk supplies in the Columbus(O.) area. The source of the antibiotics, of course, was the treatment of cattle on the farms. This survey and the study reported received particular impetus from the difficulty noted in obtaining adequate activity of bacterial cultures used to obtain cheese and other dairy products.

It was found that only 1.3 per cent of 151 raw milk individual herd samples tested contained more than critical concentrations of antibiotics as revealed by the disc assay and the acid inhibition methods. Pasteurized bulk milk samples were found to contain no detectable antibiotics.

The effect of antibiotics on the keeping quality of milk was also investigated. Streptomycin, chlortetracycline and oxytetracycline were added to milk at the rate of 1.0 and 25 μg./ml. and penicillin at the rate of 1.0 and 25 units/ml. On raw milk, none of the antibiotics in either concentration had any appreciable effect on the keeping quality. On pasteurized milk, penicillin and streptomycin increased the keeping quality by about 4 days when used in the low concentration, and by about 7 to 8 days when used in the high concentration. Chlortetracycline and oxytetracycline were more effective than the other two antibiotics and delayed the microbial spoilage of pasteurized milk by about two to three weeks.

The authors pointed out that long-term feeding trials would be necessary to determine whether or not any undesirable effects would be produced by the continued ingestion of milk containing small amounts of added antibiotics.

Therapy With Reserpine in the Female Climacteric. Kupperman, H. S., Blatt, M. H. G., Vosburgh, L. F., Canis, J., and Wetchler, B. *J. Am. Geriat. Soc. 4:*160 (1956). The effect of reserpine in the female climacteric was evaluated when combined with one or more of five different steroid hormones. The patients, numbering nearly 1400, complained of symptoms arising from either the

natural or surgical climacteric. The drug preparation was given blind, that is, neither the patient nor the physician knew which drug was being given. The severity of the complaints, as determined by interrogation of the patient, was the basis for the evaluation of the effectiveness of therapy.

Thirteen different preparations were given and evaluated. Each preparation contained one or more of the following drugs: reserpine, amphetamine sulfate, homatropine methyl bromide, ethinyl estradiol, conjugated equine estrogens, methyl testosterone, stilbestrol, diethylstilbestrol, phenobarbital, Bellafoline, ergotamine tartrate and a placebo.

The results were tabulated by the authors. They concluded that there was no synergism between reserpine and the steroid hormones administered in the control of the climacteric syndrome. The control obtained with reserpine plus an estrogen was not comparable to that obtained with the estrogen alone. The authors also noted that the combination of reserpine with estrogens provides an inflexible preparation, the dosage of which cannot be adjusted to the needs of the individual patient. Such a combination does not permit regulation of the contents should untoward reactions to one component be noted. Untoward reactions to reserpine were noted in some patients. In a few patients, reserpine was combined with amphetamine sulfate and homatropine methyl bromide in order to try to reduce the excessive sedation and/or the nasal stuffiness. There did not appear to be any appreciable benefit from such combinations.

The Analgesic Potency and Side Effects of Dihydrocodeine and Dihydroisocodeine. Gravenstein, J. S., Smith, G. M., Sphire, R. D., Isaacs, J. P., and Beecher, H. K. *New England J. Med. 254:877* (1956). Dihydrocodeine and dihydroisocodeine are hydrogenated derivatives of codeine and isocodeine, respectively. The analgesic potency of these compounds were evaluated in patients with postoperative wound pain. The evaluation of side effects was made with normal volunteers.

The authors found that dihydrocodeine and dihydroisocodeine were both potent analgesic agents. In a dose of 30 mg. per 70 Kg.

of body weight they were approximately equivalent in analgesic effect to 10 mg. of morphine per 70 Kg. of body weight. All three compounds were administered subcutaneously. Only paired data were used for comparison of pain-relieving power, that is, doses of morphine and one of the other analgesic agents were administered to the same patient as successive medications for pain. The patients were unaware of the name of the drug administered in any particular case.

While dihydrocodeine and dihydroisocodeine were approximately equal to morphine in analgesic potency, there was a difference in side effects. Dihydroisocodeine was approximately equal to morphine, in the dose given above, in the incidence and degree of side effects. However, dihydrocodeine was practically devoid of side effects. The side effects of respiratory depression, sleepiness, mental confusion, sluggishness, dysphoria, and nausea, present to a significant degree with both morphine and dihydroisocodeine, were not present to an appreciable degree with dihydrocodeine.

Dihydrocodeine was of somewhat shorter duration of action than morphine, but this was not of practical importance since the side effects were so few and slight that the drug can be readministered.

The authors attempted to employ a more precise evaluation of the psychologic effects of the agents studied and a modified technique in the appraisal of analgesic potency, that has been carried out previously for analgesic agents.

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